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Transgenic rabbits with lymphocytic leukemia induced by the c-myc oncogene fused with the immunoglobulin heavy chain enhancer.

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Transgenic rabbits with the rabbit c-myc oncogene fused with the rabbit immunoglobulin heavy chain enhancer region (E mu) DNA were developed by microinjecting pronuclei of single cell zygotes with the gene construct and implanting the microinjected eggs into pseudopregnant females. At age 17-20 days, 3 of 21 offspring born to seven females were found to have peripheral blood leukocyte counts of greater than 100,000 per mm3. Histology analyses showed extensive lymphocytic infiltration in the liver and kidney, indicating that these rabbits had a malignant lymphocytic leukemia. Genomic DNA analyses of thymus and peripheral blood lymphocytes revealed that the leukemic rabbits were transgenic and that both immunoglobulin heavy and kappa light chain genes were rearranged in the leukemic cells; thus, the leukemic cells are of B-cell lineage. One to four heavy and light chain gene rearrangements were observed, suggesting that the B-cell tumors were oligoclonal. Stable tissue culture cell lines from the bone marrow and peripheral blood of one of the transgenic rabbits have been developed. The development of B-cell leukemias in rabbits with the E mu-myc transgene contrasts with the development of B-cell lymphomas in mice carrying a similar transgene. The lymphomas in mice develop in adults and are monoclonal in origin. The leukemias in rabbits develop in juveniles, less than 3 weeks after birth, and appear oligoclonal in origin. The leukemias seem to develop in rabbit at a specific stage of development, and we suggest that a normal developmental signal may be involved in the oncogenesis.

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